

FORM PTO-1390 (Modified)
(REV 11-2000)

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

ATTORNEY'S DOCKET NUMBER

**TRANSMITTAL LETTER TO THE UNITED STATES
DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371**

602-1539

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR 1.5)

09/914803

INTERNATIONAL APPLICATION NO.
PCT/GB00/00212

INTERNATIONAL FILING DATE
January 25, 2000

PRIORITY DATE CLAIMED
March 16, 1999

TITLE OF INVENTION

Sample Imaging

APPLICANT(S) FOR DO/EO/US

John Gordon Kushbrooke and Claire Elizabeth Hooper

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (24) indicated below
4. ☒ The US has been elected by the expiration of 19 months from the priority date (Article 31)
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
 - a. ☐ is attached hereto (required only if not communicated by the International Bureau).
 - b. ☒ has been communicated by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)
6. ☐ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2))
 - a. ☐ is attached hereto
 - b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
 - a. ☒ are attached hereto (required only if not communicated by the International Bureau)
 - b. ☒ have been communicated by the International Bureau
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired
 - d. ☐ have not been made and will not be made
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
10. ☐ An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).
11. ☒ A copy of the International Preliminary Examination Report (PCT/IPEA/409)
12. ☐ A copy of the International Search Report (PCT/ISA/210).

Items 13 to 20 below concern document(s) or information included:

13. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included
15. ☒ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment
17. ☐ A substitute specification
18. ☐ A change of power of attorney and/or address letter
19. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter 2 and 35 U.S.C. 1.821 - 1.825
20. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4)
21. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
22. ☐ Certificate of Mailing by Express Mail
23. ☐ Other items or information:

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR 1.5) <div style="font-size: 24pt; font-weight: bold; text-align: center;">09/914803</div>		INTERNATIONAL APPLICATION NO <div style="font-weight: bold; text-align: center;">PCT/GBOO/00212</div>		ATTORNEY'S DOCKET NUMBER <div style="font-weight: bold; text-align: center;">602-1539</div>	
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24. The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :

- ☒ Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO \$1000.00
- ☐ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO \$860.00
- ☐ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$710.00
- ☐ International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) \$690.00
- ☐ International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) \$100.00

ENTER APPROPRIATE BASIC FEE AMOUNT =

Surcharge of \$130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (e))

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	19 - 20 =	0	x \$18.00		\$0.00
Independent claims	2 - 3 =	0	x \$80.00		\$0.00
Multiple Dependent Claims (check if applicable) <input type="checkbox"/>					\$0.00
TOTAL OF ABOVE CALCULATIONS =					\$860.00
<input type="checkbox"/> Applicant claims small entity status. (See 37 CFR 1.27). The fees indicated above are reduced by 1/2					\$0.00
SUBTOTAL =					\$860.00
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492 (f))					\$0.00
TOTAL NATIONAL FEE =					\$860.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) (check if applicable). <input type="checkbox"/>					\$0.00
TOTAL FEES ENCLOSED =					\$860.00
					Amount to be: refunded \$
					charged \$

CALCULATIONS PTO USE ONLY

a. ☒ A check in the amount of \$860.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No _____ in the amount of _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No 12-0913 A duplicate copy of this sheet is enclosed

d. ☐ Fees are to be charged to a credit card **WARNING:** Information on this form may become public **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO

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SIGNATURE

William M. Lee, Jr.
 NAME

26,935
 REGISTRATION NUMBER

08/29/2001
 DATE

09/914803

JC03 Rec'd PCT/PTO 29 AUG 2001

602-1539

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE THE APPLICATION OF)
Cambridge Imaging Limited et al.)
)
)
SERIAL NO.: TO BE ASSIGNED)
)
FILED: HEREWITH)
)
FOR: SAMPLE IMAGING)

AMENDMENT ACCOMPANYING APPLICATION

Honorable Director of Patents and Trademarks
Washington, D.C. 20231

Dear Sir,

The present application is the national filing of international application number PCT/GB00/00212. Appended hereto is a copy of the international preliminary examination report for this application, having appended thereto the claims as they currently appear in the international application. Before calculation of the national filing fee for the United States, it is requested that the application be amended as follows:

In the claims

Amend claims 3,4,6-9, and 11-17 as follows:

3. (Amended) A system according to claim 1, wherein the CCD camera is a bare cooled CCD camera or an intensified CCD camera.

4. (Amended) A System according to claim 2, wherein a shutter or iris is included in the light path between the sample and the CCD camera.
6. (Amended) A system according to claim 4, wherein the shutter is located between any pair of components of the multi-component lens.
7. (Amended) A system according to claim 1, wherein the entire sample plate is imaged and analysed in a single exposure.
8. (Amended) A system according to claim 1, wherein part of the sample plate is imaged at a time, so that the whole plate can be imaged and analysed by means of multiple exposures.
9. (Amended) A system according to claim 1, wherein the complex lens comprises an imaging lens located close to the sample and a field lens located close to the taper input.
11. (Amended) A system according to claim 9, wherein efficient light gathering is achieved by bringing the sample plate as close as possible to the imaging lens and arranging the lens powers to cause the cone of light entering the fibre optic taper at least substantially to fill the numerical aperture (NA) of the taper.
12. (Amended) A system according to claim 9, wherein the light gathering efficiency is of the order of 3.5%.

13. (Amended) A system according to claim 1, wherein the taper gives a demagnification of the order of 2.87.

14. (Amended) A system according to claim 9, wherein the imaging lens has a numerical aperture sufficiently large to fill the numerical aperture of the taper.

15. (Amended) A system according to claim 1, wherein the complex lens is designed also to be telecentric at its input.

16. (Amended) A system according to claim 9, wherein the complex lens also includes a second field lens mounted close to the sample plate a select rays generally normal to the plate, even near to the edge of the plate, and thereby minimize parallax effects.

17. (Amended) A system according to claim 1, using a laser light source to illuminate the sample.

REMARKS

The above amendments are being made in order to eliminate multiple dependency and improper multiple dependency before calculation of the national filing fee for the United States. Should any multiple dependency remain, that is unintended, and the Patent and Trademark Office is requested to cancel any remaining multiple dependent claims without prejudice before calculation of the national filing fee.

Examination of the application on its merits is awaited.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

3. (Amended) A system according to claim 1 [or claim 2], wherein the CCD camera is a bare cooled CCD camera or an intensified CCD camera.
4. (Amended) A System according to [any of claims 1 to 3] claim 2, wherein a shutter or iris is included in the light path between the sample and the CCD camera.
6. (Amended) A system according to claim 4 [when appendant to claim 2], wherein the shutter is located between any pair of components of the multi-component lens.
7. (Amended) A system according to [any of claims 1 to 6] claim 1, wherein the entire sample plate is imaged and analysed in a single exposure.
8. (Amended) A system according to [any of claims 1 to 6] claim 1, wherein part of the sample plate is imaged at a time, so that the whole plate can be imaged and analysed by means of multiple exposures.
9. (Amended) A system according to [any of claims 1 to 8] claim 1, wherein the complex lens comprises an imaging lens located close to the sample and a field lens located close to the taper input.
11. (Amended) A system according to claim 9 [or claim 10], wherein efficient light gathering is achieved by bringing the sample plate as close as possible to the imaging lens and arranging

the lens powers to cause the cone of light entering the fibre optic taper at least substantially to fill the numerical aperture (NA) of the taper.

12. (Amended) A system according to [any of claims 9 to 11] claim 9, wherein the light gathering efficiency is of the order of 3.5%.
13. (Amended) A system according to [any of claims 1 to 12] claim 1, wherein the taper gives a demagnification of the order of 2.87.
14. (Amended) A system according to [any of claims 9 to 13] claim 9, wherein the imaging lens has a numerical aperture sufficiently large to fill the numerical aperture of the taper.
15. (Amended) A system according to [any of claims 1 to 14] claim 1, wherein the complex lens is designed also to be telecentric at its input.
16. (Amended) A system according to claim 9[or any claim appendant thereon], wherein the complex lens also includes a second field lens mounted close to the sample plate a select rays generally normal to the plate, even near to the edge of the plate, and thereby minimize parallax effects.
17. (Amended) A system according to [any of claims 1 to 12] claim 1, using a laser light source to illuminate the sample.

Title: Sample imaging

Field of invention

This invention concerns optical systems for imaging multiwell sample plates and the like onto camera devices, for analysis and monitoring of light activity in the wells.

Background to the invention

Biomedical samples, typically in multiwell sample plates, can be viewed and measured with a CCD camera using a suitable lens. The lens demagnification can be chosen to match the size of the whole sample plate (eg typically 110mm x 75mm), or a part of it, to the CCD. The CCD camera can be either a bare cooled CCD, or an image intensified CCD.

Typically a CCD camera sensor is 1" (25mm) square. A demagnification of $\sim 110/25=4.4$ is therefore necessary to view a whole sample plate.

In modern biomedical assay chemistries where luminescent or fluorescent light emission occurs at long wavelengths towards the red end of the spectrum (600-700nm) a bare cooled CCD has a great advantage. The CCD is cooled by Peltier or Cryogenic means to reduce the dark noise of the CCD sufficiently. Special electronics is needed to minimise read-out noise, but very low light levels can then be detected in the presence of low noise. The quantum efficiency of a CCD over most of the visible range is 35-40%. Using a thinned back-illuminated CCD, the efficiency can be as high as 80-90%.

The situation can be contrasted with image intensified CCD cameras, where photons are detected in the photocathode of the image intensifier. The quantum efficiency of typical low-noise photocathodes in the red is relatively poor (<5%). Where Gen1

image intensifiers are used, there is also usually shading, ie a fall-off of detection efficiency away from the centre of the field of view. Where Gen2 (microchannel plate) image intensifiers are used, there is also a problem at medium and high light levels, where the tube lifetime becomes limited. Gen3 image intensifiers offer much improved quantum efficiency in the red, but these are to some extent in the development stage, at least where tubes of reasonable diameter (eg 40mm) are involved, and the noise level can be a problem.

With an image intensified CCD a single detected photon results in a burst of electrons in the CCD, spread over a number of pixels. Centroiding methods have been proposed to achieve sub-pixel spatial resolution (eg of the order of 10 microns) for locating the coordinates of a detected photon which is important in some imaging applications where many tiny light emitting sites are present in the sample, and the imaging process requires the different light emitting sites to be resolved the one from the other.

In general, centroiding methods cannot be used with a bare cooled CCD because a detected photon results in only a single electron in the silicon.

Instead of using a lens for imaging, a fibre optic taper can be employed to image the sample plate onto the CCD. A disadvantage however, is that multiple exposures are required to cover the entire plate.

The invention

According to one aspect of the present invention, a sample plate is imaged onto a CCD camera by the optical combination of at least one lens and a fibre-optic taper. A fibre optic taper possess some advantages and the use of a converging lens possesses other advantages. As will be apparent from later description however, the invention is able to achieve more than

cone of light entering the fibre optic taper just to fill the numerical aperture (NA) of the taper.

In a first preferred embodiment, the taper is 110mm diameter with a demagnification of 2.87. Lenses having an aperture of the order of F1.1 or better are preferred.

In general, the imaging lens will be a complex lens consisting of a number of separate lens components.

Preferably the light source is a laser light source.

In a further preferred arrangement a second field lens may be mounted close to the sample plate to select rays generally normal to the plate, even near to the edge of the plate, and thereby minimise parallax effects.

Either or both of the field lenses may be a simple single element lens or to advantage may be a multi-element lens.

In general, the imaging and field lenses will comprise a single, multi-component system possessing the property of telecentricity at object and image ie the ability to select rays that are on average normal to the object and image is parallax free.

Description of examples

In the accompanying drawings:

Figures 1(a), (b) and (c) are provided to draw schematically a comparison between different possible arrangements; and

Figures 2 and 3 show differing possible practical embodiments of a system embodying the invention.

It is assumed in Figures 1(a) and 1(c) that the lenses can be

high quality multi-component lenses.

An example of one arrangement known in principle uses a bare cooled CCD and is shown schematically in Figure 1(a). It uses a lens 10 to image the sample plate 12 onto the CCD 14. A typical 1" CCD will have 1024x1024 pixels, the pixels being of size 24 microns x 24 microns. A shutter 16 (or iris) is shown included in the light path to protect the CCD if a strong light source eg a laser, is being used to excite fluorescence in the sample, particularly if a time-resolved fluorescence method is being used (ie light on, light off, read sample, repeat).

In other circumstances, the shutter or iris may be employed to reduce frame shift smear such as when using self luminescent samples.

A generally known alternative to lens imaging is contact imaging, in which the sample plate 12 is presented directly to the CCD, via either a one-to-one thin fibre-optic plate to which the CCD may be bonded, or via a demagnifying taper to which the CCD may be bonded. This is shown in Figure 1(b), in which a taper 18 (typically having an input diameter of 78mm) enables a plate 12 to be viewed in four shots (or exposures). Contact imaging is to be preferred where higher light capture efficiency is desired. Figure 1(b) shows a bare cooled CCD 14 but an image intensified CCD could instead be used.

The relative light gathering efficiency of lens imaging and taper contact imaging is also shown in Figures 1(a) and 1(b). In the case of a lens, the standard formula (in terms of the demagnification m and the ratio F of focal length:diameter) given in Figure 1(a) applies. This means that in the example given an overall efficiency of only about 0.7% is obtained even with a very high quality F1.1 lens. The lens has the advantage that it can view the sample in one go. Also a shutter can be included as mentioned above. With taper contact imaging as depicted in Figure 1(b), an efficiency of about 3% is

wells of a sample plate.

Figure 3 shows a second field lens 32 mounted just beneath the sample plate 26 which collects rays that are on average normal to the plate. This collection of normal rays occurs across the whole area of the plate, even at the edges. As described above this telecentric arrangement minimises parallax effects, which can make it difficult otherwise to gather light from deep down a sample plate well. The imaging techniques illustrated here may be used to advantage in systems for analysing photon emitting assays such as described in UK Patent Specification No. 2294319.

It is to be noted that, in Figure 2, the focal length and relative apertures are indicated, as well as the axial separator of the component. The corresponding details of the arrangement shown in Figure 3 are readily calculatable, but will not be the same as the details marked in Figure 2.

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JC03 Rec'd PCT/FTO 29 AUG 2001

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CLAIMS

1. An optical system for imaging a sample plate onto a camera device, wherein the sample plate is imaged into a CCD camera by the optical combination of at least one lens through which light enters a fibre-optic taper, characterised in that the lens is a complex lens designed to be telecentric at least at its output, whereby light enters the taper at any point of its input face on average normal thereto.
2. A system according to claim 1, wherein the lens is a multi-component lens.
3. A system according to claim 1 or claim 2, wherein the CCD camera is a bare cooled CCD camera or an intensified CCD camera.
4. A system according to any of claims 1 to 3, wherein a shutter or iris is included in the light path between the sample and the CCD camera.
5. A system according to claim 4, wherein the shutter is located between the lens and the taper input, or between the sample and the lens.
6. A system according to claim 4 when appendant to claim 2, wherein the shutter is located between any pair of components of the multi-component lens.
7. A system according to any of claims 1 to 6, wherein the entire sample plate is imaged and analysed in a single exposure.
8. A system according to any of claims 1 to 6, wherein part of the sample plate is imaged at a time, so that the whole plate can be imaged and analysed by means of multiple exposures.

9. A system according to any of claims 1 to 8, wherein the complex lens comprises an imaging lens located close to the sample and a field lens located close to the taper input.
10. A system according to claim 9, wherein the field lens acts to bend the light rays so as to be on average normal to the taper, hence minimising any loss of light due to rays entering the taper at angles outside the maximum acceptable angle $\theta = \sin^{-1}(\text{NA})$, where NA is the numerical aperture of the taper, (equal to the magnification).
11. A system according to claim 9 or claim 10, wherein efficient light gathering is achieved by bringing the sample plate as close as possible to the imaging lens and arranging the lens powers to cause the cone of light entering the fibre optic taper at least substantially to fill the numerical aperture (NA) of the taper.
12. A system according to any of claims 9 to 11, wherein the light gathering efficiency is of the order of 3.5%.
13. A system according to any of claims 1 to 12, wherein the taper gives a demagnification of the order of 2.87.
14. A system according to any of claims 9 to 13, wherein the imaging lens has a numerical aperture sufficiently large to fill the numerical aperture of the taper.
15. A system according to any of claims 1 to 14, wherein the complex lens is designed also to be telecentric at its input.
16. A system according to claim 9 or any claim appendant thereon, wherein the complex lens also includes a second field lens mounted close to the sample plate to select rays generally normal to the plate, even near to the edge of the plate, and thereby minimise parallax effects.

17. A system according to any of claims 1 to 12, using a laser light source to illuminate the sample.

18. A system according to claim 16, wherein both field lenses are multi-element lenses.

19. A system for imaging a whole sample plate, or part thereof, comprising at least one complex lens through which light enters a fibre optic taper, wherein the lens is telecentric at least at its output and the power of the lens receiving light from the sample plate is arranged to cause the cone of light entering the taper to fall within the numerical aperture of a taper, the output face of which is bonded to a CCD camera.



PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

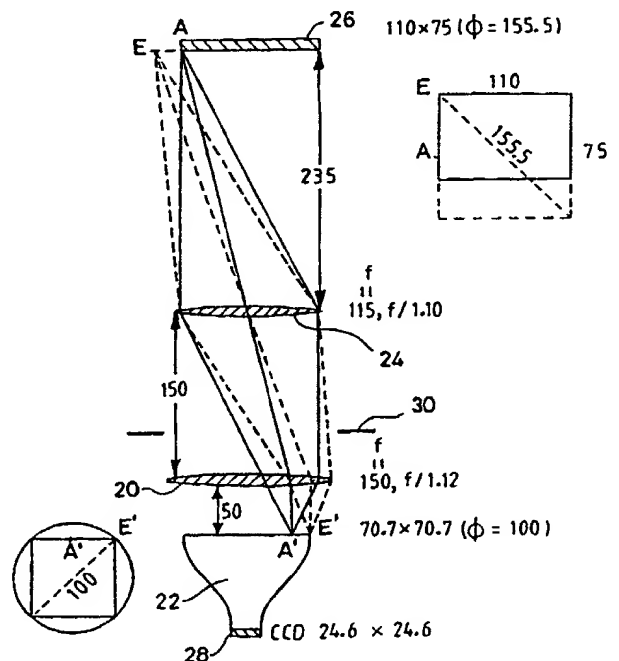
(51) International Patent Classification ⁷ : G01N 21/25, G02B 6/06	A1	(11) International Publication Number: WO 00/55601 (43) International Publication Date: 21 September 2000 (21.09.00)
<p>(21) International Application Number: PCT/GB00/00212</p> <p>(22) International Filing Date: 25 January 2000 (25.01.00)</p> <p>(30) Priority Data: 9905954.5 16 March 1999 (16.03.99) GB</p> <p>(71) Applicant (for all designated States except US): CAMBRIDGE IMAGING LIMITED [GB/GB]; St. John's Innovation Centre, Cowley Road, Cambridge CB4 4WS (GB).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): <u>RUSHBROOKE, John</u>, Gordon [GB/GB]; 10 Barrington House, Southacre Park, Southacre Road, Cambridge CB2 2TY (GB). <u>HOOPER, Claire, Elizabeth</u> [GB/GB]; 5 Rotherwick Way, Cambridge CB1 4RX (GB). <i>Co BY</i></p> <p>(74) Agent: KEITH W NASH & CO.; 90-92 Regent Street, Cambridge CB2 1DP (GB).</p>	<p>(81) Designated States: JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p>Published With international search report.</p>	

(54) Title: SAMPLE IMAGING

(57) Abstract

An optical system for imaging a multiwell sample plate onto a CCD camera, wherein light from the illuminated sample plate (26) is imaged by one or more lenses (20, 24) onto a fibre optic taper (22), bonded to the input face of the camera (28).

Lens-Taper
Viewing whole plate (Schematic)



Distance Plate to Taper = 434 mm

1 / 3

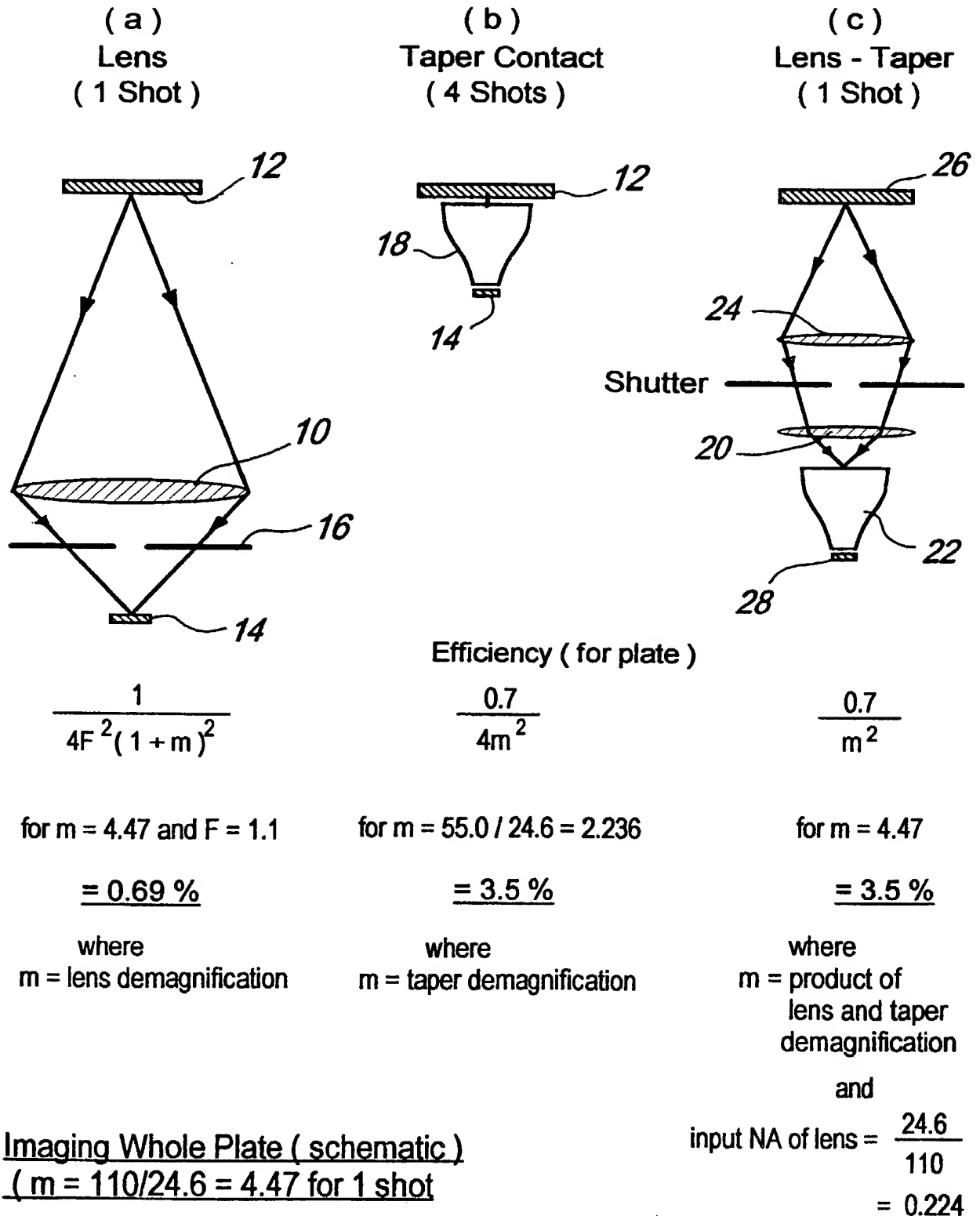


Fig. 1

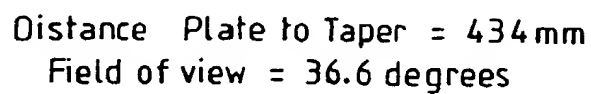
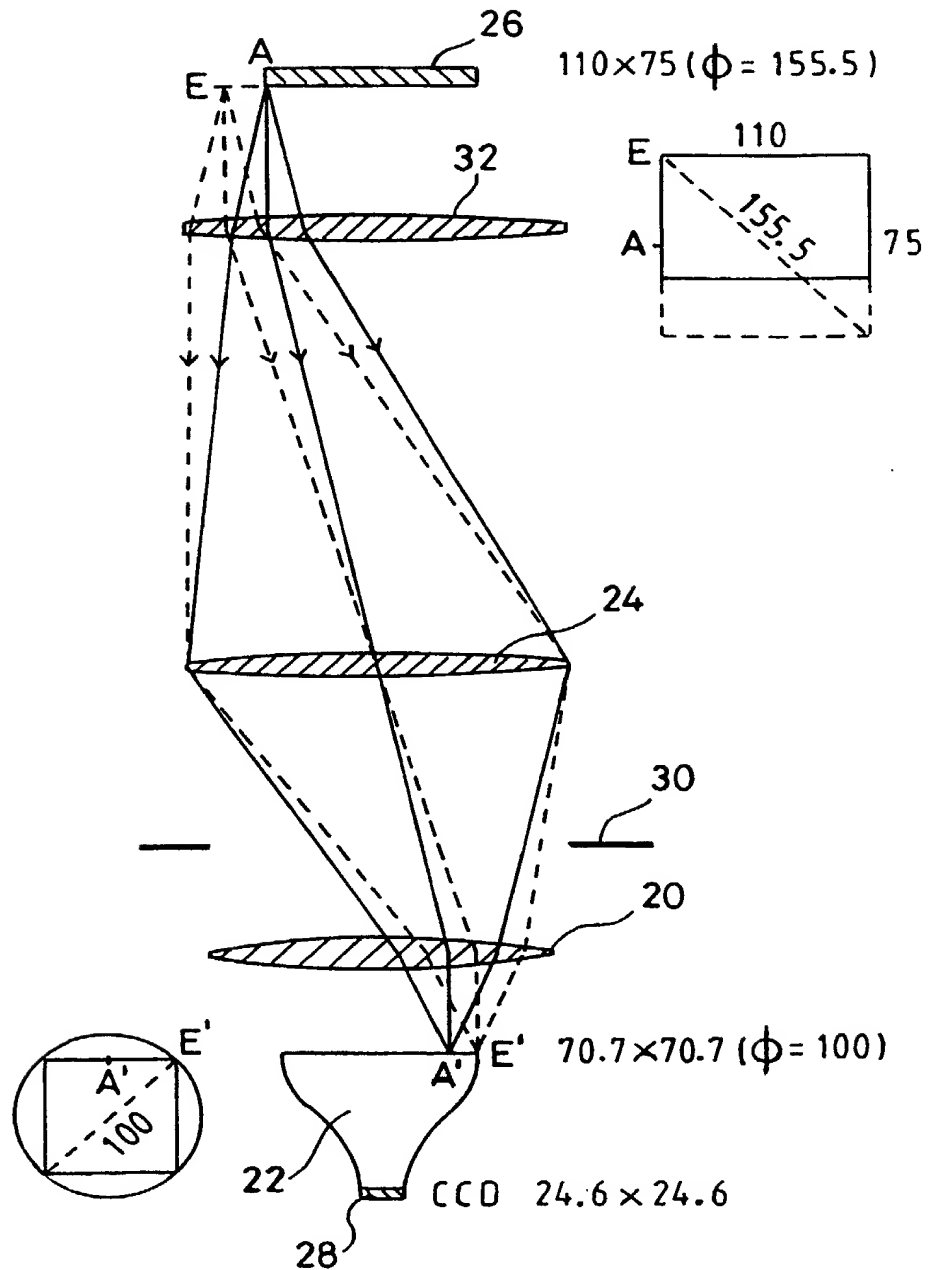


Fig.2

3 / 3



Lens Taper
Viewing whole plate (Schematic)

Fig.3

602-1539

DECLARATION FOR PATENT APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled **SAMPLE IMAGING**, the specification of which:

___ is attached hereto; or

X was filed on 25 January 2000 as United States Application Number
or PCT International Application Number PCT/GB00/00212
and was amended on 1 March 2001 (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 C.F.R. 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application for patent or inventor's certificate or any PCT international application having a filing date before that of the application on which priority is claimed.

PRIOR FOREIGN APPLICATION(S)

<u>9905954.5</u>	<u>Great Britain</u>	<u>March 16, 1999</u>	Priority Claimed
(Application Number)	(Country)	(Filing Date)	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<u> </u>	<u> </u>	<u> </u>	<input type="checkbox"/> Yes <input type="checkbox"/> No
(Application Number)	(Country)	(Filing Date)	

I hereby claim the benefit under 35 U.S.C. 119(e) of any United States provisional application(s) listed below.

PRIOR U.S. PROVISIONAL APPLICATION(S)

<u> </u>	<u> </u>
(Application Number)	(Filing Date)
<u> </u>	<u> </u>
(Application Number)	(Filing Date)

I hereby claim the benefit under 35 U.S.C. 120 of any United States application(s), or 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application in the manner provided by the first paragraph of 35 U.S.C. 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 C.F.R. 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. OR PCT PARENT APPLICATION(S)

<u>PCT/GB00/00212</u>	<u>January 25, 2000</u>	<u>Pending</u>
(Application Number)	(Filing Date)	(Patent Number, if any)
<u> </u>	<u> </u>	<u> </u>
(Application Number)	(Filing Date)	(Patent Number, if any)

I hereby appoint the following registered practitioners to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Thomas E.

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Smith, Registration No. 18,243; Dennis M. McWilliams, Registration No. 25,195; James R. Sweeney, Registration No. 18,721; William M. Lee, Jr., Registration No. 26,935; Glenn W. Ohlson, Registration No. 28,455; David C. Brezina, Registration No. 34,128; Jeffrey R. Gray, Registration No. 33,391; Gerald S. Geren, Registration No. 24,528; Robert F. I. Conte, Registration No. 20,354; Timothy J. Engling, Registration No. 39,970; Peter J. Shakula, Registration No. 40,808; Howard B. Rockman, Registration No. 22,190; John W. Hayes, Registration No. 33,900; Mark A. Hagedorn, Registration No. 44,731; and Mark J. Nahnsen, Registration No. 51,093.

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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Signature C. E. Hooper Date 25 April 2002
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